

BLOOD UREA CLEARANCE IN INDIAN WOMEN WITH NORMAL MENSTRUATION, AND IN NORMAL AND TOXAEMIC PREGNANCY

by

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It has been observed that in normal pregnancy, not only that there is a diminution in total nitrogen excretion, but the proportion of urea nitrogen excretion to that of total nitrogen excretion is lowered. (de Wesselow 1922). As regards the kidney function the evidence is conflicting. Hurwitz and Ohler (1932), Cantarow and Ricchiuti (1933) and Nice (1935) showed that the kidney function as indicated by blood urea clearance test (Moller, McIntosh and Van Slyke 1929) is somewhat affected during normal and toxæmic pregnancy, while Dieckman (1935) observed otherwise. The results presented by Standar, Ashton and Cadden (1932) have been based on the examination of a very small number of subjects and are not decisive. Nayar (1940) has presented data for normal pregnancy in Indian subjects in Madras. It will be seen that no definite confirmative and sufficient experimental evidence has been available to show whether blood urea clearance is at all affected during

normal and toxæmic pregnancy. The present study was therefore undertaken.

As the investigation was to be done on Indian subjects, it was first necessary to study the blood urea clearance in normal menstruating Indian women, so as to be able to have standard clearance values for use for the evaluation of kidney function by the use of blood urea clearance test (Moller et. al. Loc cit). That the use of Van Slyke standard values for the blood urea clearance, which are based on the study of American normal subjects, in the case of Indian subjects, leads to misleading results has been shown by Gokhale (1941) in his study of blood urea clearance in Indian subjects. He showed that the blood urea clearance values in normal Indian men are much lower than those obtained for normal American subjects (Moller et al. loc cit) and used for evaluation of kidney function. Similar results have been obtained by Srikantia and Shamanna (1944), by Pai (1945) and Nadkarni, Chitre and Monterio (1955) for Indian subjects.

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Material and Methods

In the present investigation blood urea clearance was studied in normal menstruating, normal pregnant, post-

delivery, normal and toxæmic conditions in Indian women. The normal subjects, mostly nurses from the Wadia Maternity Hospital, Bombay, and other private hospitals, were healthy young women with normal menstruation. The normal pregnancy, post-delivery and toxæmic pregnancy subjects were from Wadia Maternity Hospital. The ages of these subjects ranged from 20 to 35 years. The diet of the subjects was a mixed one, mostly vegetarian with little meat occasionally. All the subjects consumed milk. The subjects were hospitalized at least a day preceding the test. The blood urea

height and the blood pressure were recorded.

Results and Discussion

Blood Urea Clearance in Normal Menstruating Women: Out of 41 subjects examined, 33 subjects were of maximum clearance, the volume of urine per minute being more than 2.0 ml., while 8 were of standard clearance, the volume of urine per minute being less than 2.0 ml. The test was performed 10 days after the menstrual period. The subjects had normal blood pressure. The results of these subjects are given in Table No. I.

TABLE I

	For 33 subjects of maximum clearance V 2.0ml/min.	For 8 subjects of standard clearance V 2.0ml/min.
(1) Body weight in kilos	222.4	216.8
(2) Height cms.	152.5	150.0
(3) Body surface area/sq.m.	1.40	1.34
(4) Urine volume ml./min. (V)	2.52	1.52
(5) Urine urea N mg% (U)	159.7	255.7
(6) Blood urea N mg% (B)	12.21	12.53
(7) Blood urea clearance		
UV		
Maximum clearance Cm: $\frac{UV}{B}$ ml	32.95	—
U√V		
Standard clearance Cs: $\frac{U\sqrt{V}}{B}$ ml	—	25.15
(8) Range	48.21 to 25.54	40.48 to 15.54
(9) Standard deviation	± 4.496	± 7.044
(10) Standard error	0.7825	2.492
(11) % of subjects within significant variation range	82.5	—
(12) Clearance values corrected to body surface area 1.73 sq.m.	40.72	31.68

clearance test was carried out according to Moller et al. (loc cit) and Gokhale (loc cit). The blood urea nitrogen was determined according to Karr (1944). The body weight,

The blood urea nitrogen average for all the 41 normal menstruating Indian subjects studied in this series is 12.2 mg. 100 ml. with a range of 10.00 to 15.6 mg. per cent. While no

data are available for normal Indian women, the average obtained is not very different from that obtained for normal Indian men viz. 12.56 mg. per cent (range 9.0 to 14.9 mg. per cent) by Gokhale (loc cit) and also the average figure of 12 mg. per cent (range 9.0 to 15 mg. per cent) for normal European and American men: Folin (1930) and Berglund (1922). Srikantia and Shamanna (loc cit) and Pai (loc cit) obtained averages of 14.6 mg.% 10.4 mg.% respectively in their studies on normal Indian subjects.

The average values obtained for blood urea clearance in the present study were 32.95 ml. for maximum clearance (Cm) for 1.40 sq. m. body surface area and 25.15 ml. for standard clearance (Cs) for 1.34 sq. m. body surface area. When calculated to 1.73 sq. m. body surface area for comparison, the maximum clearance comes to 40.72 ml. and standard

40.0 ml. for maximum clearance (Cm) for 1.57 sq. m. body surface area and 31.5 ml. for standard clearance (Cs) for 1.61 sq. m. body surface area or 44.0 ml. for maximum clearance (Cm) and 33.8 ml. for standard clearance (Cs) when corrected to body surface area of 1.73 sq. m. It has been observed by Gokhale (loc cit) that the blood urea clearance values for normal Indian men are about 60% lower than those obtained for normal Americans (Moller et al. loc cit) viz. Cm. 75 ml. and Cs. 54 ml. used as standards. This is due to lower urinary nitrogen excretion by Indians, probably due to their low protein intake. Similar low blood urea clearance values were obtained by other workers viz. Srikantia and Shamanna (loc cit) Pai (loc cit) and Nadkarni et al. (loc cit) as stated before. Table II gives the blood urea clearance values by various workers for comparison.

TABLE II

Blood Urea Clearance Corrected to 1.73 sq.m. Body Surface Area For Normal Indian Men and Women and American Men

	Maximum clearance ml (Cs)	Standard clearance ml (Cm)
(1) Normal Indian Women		
Present Study	40.7	31.7
(2) Normal Indian Men		
Gokhale (loc cit)	44.0	33.8
Nadkarni et al. (loc cit)	49.0	38.4
Srikantia et al. (loc cit)	52.6	39.4
Pai (loc cit)	—	35.2
(3) Normal American Men		
Moller et al. (loc cit)	75.0	54.0

clearance to 31.68 ml. The average clearance values obtained for normal Indian men by Gokhale (loc cit) were

The average blood urea clearance values for normal Indian women are lower than those for normal European

or American men. As no data have been available for blood urea clearance for normal European women for evaluation of kidney function, the average clearance values for normal European men have been used for comparison in case of women. It can be observed from Table II that the blood urea clearance values for normal Indian women do not significantly differ from those of normal Indian men and are similarly lower by about 55 to 60% than those of the average values for American men, used as standards for the evaluation of kidney function. It is evident that the use of American standards for Indian subjects would lead to incorrect evaluation of the kidney function. Hence average blood urea clearance values for normal Indian women obtained in the present study were

used for comparison in the study of blood urea clearance in normal and toxæmic pregnancy subjects.

Blood Urea Clearance in Normal Pregnancy and Post-delivery

Out of 148 subject of normal pregnancy studied for blood urea clearance, 113 were between 6th and 9th month and the rest 35 were post-delivery subjects. Out of 113 pregnant subjects, 100 were of maximum clearance and 13 were of standard clearance. The 35 normal post-delivery subjects were examined within 10 days after delivery. These subjects had no post-delivery complications at all. Out of these 35 subjects, 32 gave maximum clearance while remaining 3 gave standard clearance. The results obtained are given in Table III.

TABLE III
Maximum Clearance

Month	No. of cases	Urine volume ml/min. V	Urine urea nitrogen mg.± U	Blood urea N mg.% B	Urea clear-	Standard deviation	Standard error
					ance UV		
6th	26	2.59	166.9	13.16	32.87	5.764	1.131
7th	29	2.60	159.7	12.71	32.60	5.353	0.994
8th	23	2.50	171.2	12.56	34.06	5.824	1.214
9th	22	2.81	153.8	12.99	33.28	4.634	0.9881
All months together	100	2.62	162.9	12.89	33.11	5.364	1.078
Post delivery	32	2.60	152.4	12.35	32.09	2.098	0.3711
Normal menstruating	33	2.52	159.7	12.21	32.95	4.496	0.7825

Standard Clearance

Month	No. of cases	Urine volume ml/min. V	\sqrt{V}	Urine urea N mg.% U	Blood urea N mg.% B	Urea clear- ance	Standard deviation	Standard error
						$\frac{U\sqrt{V}}{B}$		
6th	4	1.67	1.292	242.5	12.78	24.51	5.575	3.287
8th	4	1.53	1.237	286.7	14.25	24.88	3.397	1.698
9th	5	1.09	1.044	305.3	13.80	23.10	3.599	1.609
All months together	13	1.40	1.185	280.3	13.70	24.25	4.145	2.153
Post delivery	3	1.56	1.249	225.3	11.83	23.79	3.832	2.213
Normal menstruating	8	1.52	1.233	255.7	12.53	25.15	7.044	2.492

Statistical analysis of the results obtained according to Hill (1950), showed that the blood urea clearance average for pregnant and post-delivery normal subjects did not show any significant difference at all from the averages obtained for normal menstruating Indian subjects. There is some disagreement as to the effect of normal pregnancy on blood urea clearance. Nice (1935) reported that the urea clearance progressively increases with the progress of pregnancy while Cantarow et al. (1933)

observed in 188 cases of normal pregnancy that the urea clearance averages to 101% while Dieckman (1935) found clearance varying from 45 to 17%, concluding that the clearance is not changed at all in normal pregnancy. The urea clearance test according to Cantarow et al. (1933), Hurwitz and Ohler (1932), Nice (1935), Dieckman (1935), Edden and Cooney (1935) is helpful in differentiation of various renal disorders in pregnancy. The results of these investigators are given in Table IV.

TABLE IV

Author	No. of subjects	Urea clearance per cent	Range
Hurtwitz and Ohler (1932)	5	127	82 to 167
Stander et al. (1932)	13	99.5	92 to 110
Cantarow et al. (1933)	39	75	28 to 189
Cadden et al. (1934)	9	122.7	— —
Dieckman (1935)	27	102.3	— —
Nice (1935)	13	153	80 to 286

stated that the urea clearance progressively decreases. Chesly (1939)

According to Dunn quoted by Nice (1935) "the variations of urea clear-

ance test from month to month during pregnancy are not significant".

According to present study the clearance is not at all affected in normal pregnancy. Cantarow et al. (1933) carried out the test in 39 cases of normal pregnancy. In normal pregnancy the clearance varied from 28 to 184% of the average normal. It was normal in the first few days of gestation and diminished as pregnancy advanced, being considerably lower a few days before the onset of labour. Normal values were obtained during the early days after delivery. It will be seen from the results that no significant difference was observed in any stage of normal pregnancy not even in final stage. In absence of any data in the present study for days, it is very difficult to say if there is any change in the clearance at term as stated by Cantarow et al. (1933).

According to Nayar (1940) the kidney efficiency at full-term is very much diminished, the average being 23.21% of average normal after his study of Indian subjects in Madras. Though the average blood urea nitrogen is within the normal limits, the urinary urea concentration and urine volume are diminished and consequently the clearance is much more decreased. Nayar has used for the evaluation of his blood urea clearance results, the standards of Van Slyke and that is the reason of his getting an average of 23.21% of the average normal in Indians. The value he obtained would have been about 50% of the average normal had it been calculated on Indian standards — the average clearance of which are about 55% lower than those of American

and European standards given by Van Slyke.

It will be seen from the above that the kidney function as shown by blood urea clearance is not at all affected in normal pregnancy.

Blood Urea Clearance in Toxaemic Pregnancy in Indian Subjects

A total of 83 cases of toxaemic pregnancy were studied. Of these 65 were between 6th and 9th month of pregnancy and the rest 18 were of post-partum. Out of the 65 subjects, 51 were of maximum clearance and 14 of standard clearance. The 18 post-delivery subjects were examined for their blood urea clearance within 10 days after delivery; 13 of them gave maximum clearance while 5 gave standard clearance. The results obtained are given in Table V.

In Table VI are given the average blood urea clearance for comparison between normal and toxaemic pregnancy obtained in the present study.

McPhail (1938) writes "It is believed that toxaemia will not develop if no renal impairment of the renal function exists". Stander et al. (1932) concluded that urea clearance or other renal function tests were of real value in differentiation of the mild nephritis and toxaemias of pregnancy. According to them urea clearance below 80% is strongly indicative of renal damage. There is definite evidence according to Brown (1938) that if a low clearance occurs in a woman apparently well looking and healthy she will develop toxemia later in pregnancy. The clearance may be apparently low several months before the onset of toxemia. Hurwitz and Ohler (1932) obtained

TABLE V
Maximum Clearance

Month	No. of cases	Urine vol./min. V	Urine urea N mg.% U	Blood urea N mg.% B	Urea clear- ance	Standard deviation	Standard error
					$\frac{UV}{B}$		
6th	8	2.72	163.1	16.28	27.25	2.818	0.9965
7th	12	2.44	173.5	13.32	31.77	4.856	1.402
8th	16	2.52	160.9	14.02	28.92	5.10	1.275
9th	15	2.34	191.7	14.39	31.18	3.959	1.022
All months together	51	2.42	173.4	13.73	30.56	4.249	1.187
Post delivery	13	2.34	179.0	13.11	31.95	2.166	0.586
Normal menstruating	33	2.52	159.7	12.21	32.95	4.496	0.7825

Standard Clearance

Month	No. of cases	Urine volume ml/min. V	\sqrt{V}	Urine urea N mg.% U	Blood urea N mg.% B	Urea clear- ance	Standard deviation	Standard error
						$\frac{U\sqrt{V}}{B}$		
6th	5	1.27	1.127	283.5	16.06	19.89	3.376	1.445
8th	6	1.32	1.149	306.9	16.89	20.87	4.333	1.937
9th	3	1.32	1.149	210.5	13.43	18.01	2.544	1.469
All months together	14	1.30	1.141	277.8	15.75	20.13	3.607	1.683
Post delivery	5	1.65	1.284	241.1	15.37	20.14	2.53	1.082
Normal menstruating	8	1.52	1.233	255.7	12.53	25.15	7.044	2.492

urea clearance 111% with a range of 36 to 178%. Dieckman (1935) obtained urea clearance 50.5%, 57.4% and 57.2% in acute pre-eclampsia, toxæmia and eclampsia respectively. It can be seen from these results that Brown (1938) obtained 88% and 75% urea clearance with a range of 19 to 190% and 41 to 144% for toxæmia and eclampsia respectively.

TABLE VI
 Comparison of Blood Urea Clearance in Normal and Toxemic Pregnancy
 Maximum Clearance

Month	Toxaemic pregnancy				Normal pregnancy			
	No. of cases	Average ml/min.	Range	Standard deviation	No. of cases	Average ml/min.	Range	Standard deviation
6th	8	27.25	22.4 to 30.8	2.818	26	32.87	24.8 to 50.5	5.764
7th	12	31.77	24.5 to 43.3	4.856	29	32.60	23.3 to 50.1	5.353
8th	16	28.92	18.7 to 40.4	5.100	23	34.06	22.2 to 43.7	5.824
9th	15	31.18	20.9 to 37.6	3.959	22	33.28	24.3 to 45.4	4.634
All months together	51	30.56	18.7 to 43.3	4.249	100	33.11	24.8 to 50.5	5.964
Post delivery	13	31.95	28.0 to 32.5	2.166	32	32.10	28.8 to 46.6	2.098
<i>Standard Clearance</i>								
6th	5	19.90	15.8 to 23.7	3.376	4	24.51	13.8 to 29.6	5.575
8th	6	20.87	14.2 to 28.0	4.333	4	24.88	20.0 to 28.4	3.397
9th	3	18.01	15.1 to 21.3	2.544	5	23.10	17.9 to 27.9	3.598
All months together	14	20.13	14.2 to 28.0	3.697	13	24.25	13.8 to 28.4	4.145
Post delivery	5	20.14	15.1 to 21.5	2.530	3	23.79	19.9 to 29.2	3.832

diagnosis between normal and abnormal pregnancy is made much easier by urea clearance.

The blood urea clearance values obtained in the present study in toxæmic subjects have been found to be lower than those for normal menstruating and normal pregnancy subjects. But the statistical analysis showed that these lower values are not statistically significant to show impairment of kidneys in most of the categories of the month-wise distribution. The results obtained by some of the workers have given percentage averages varying from 57 to 111% showing that the blood urea clearance is not lowered.

Summary and Conclusion

(1) Blood urea clearance has been determined for 272 Indian women subjects.

- 41 Normal menstruating
- 113 Normal pregnancy
- 35 Normal post-delivery
- 65 Toxaemic pregnancy
- 18 Toxaemic post-delivery

(2) The blood urea clearance values obtained for normal menstruating Indian women were 32.95 ml. for maximum clearance (surface area 1.40 sq. m.) and 25.15 ml. for standard clearance (surface area 1.34 sq. m.). These agree with those obtained by other workers for normal Indian men and are about 60% lower than those of American standards.

(3) The blood urea clearance values obtained for normal and toxæmic pregnancy have been presented according to the duration of pregnancy.

(4) These results show that the blood urea clearance is not affected in normal as well as in toxæmic pregnancy. The values obtained in toxæmic pregnancy were lower than those in normal menstruating and normal pregnancy but did not show any significance statistically.

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